

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

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|--|--|---|--|
| Applicant's or agent's file reference 62816-5001WO | | Date of mailing (day/month/year) 07 APR 2005 FOR FURTHER ACTION See paragraph 2 below | |
| International application No. PCT/US04/35466 | International filing date (day/month/year) 25 October 2004 (25.10.2004) | Priority date (day/month/year) 24 October 2003 (24.10.2003) | |
| International Patent Classification (IPC) or both national classification and IPC IPC(7): G01N 27/26, 27/447 and US Cl.: 204/518, 548, 627, 644 | | | |
| Applicant THE TEXAS A&M UNIVERSITY SYSTEM | | | |

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| | |
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| Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230 | Authorized officer Jeffrey T. Barton Telephone No. (571)272-1307 <div style="text-align: right; margin-top: 10px;"> <i>Jean Proctor</i> <i>Paralegal</i> </div> |
|--|---|

Form PCT/ISA/237 (cover sheet) (January 2004)

DOCKETED

By LLK Date 4/15

WO due - 7/7/05

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims 1-59

YES

Claims NONE

NO

Inventive step (IS)

Claims NONE

YES

Claims 1-59

NO

Industrial applicability (IA)

Claims 1-59

YES

Claims NONE

NO

2. Citations and explanations:

Please See Continuation Sheet

**WRITTEN OPINION OF THE
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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claims 14 and 25 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: the word "weekly" is used, though "weakly" was apparently intended.

Claim 59 is objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: it is an exact duplicate of claim 58.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 57-59 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because they are indefinite for the following reason(s): "substantially as shown and described" does not adequately define what is claimed as the invention.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 1-4, 6-14, 16-19, 21-25, 27-50, 55, and 56 lack an inventive step under PCT Article 33(3) as being obvious over Sammons et al in view of Tarnopolsky.

Regarding claims 1, 16, and 50, Sammons et al disclose an electrophoresis apparatus, comprising: an anode and cathode disposed in respective compartments as claimed (Figure 5, 61 and 64) with means for solution addition and removal (e.g. Figure 2, lines 11 and 13) and dimensions as claimed; ion-permeable barriers that prevent convective mixing (17) disposed between compartments; separation compartments disposed between the electrode compartments (Figure 5); and with a portion of each compartment (Cooling lines 14) made from a heat-conductive material, optionally ceramic. (Column 5, lines 49-55)

Tarnopolsky discloses a membrane separation apparatus in which coolant is flowed through hollow silica fibers in the chambers. (Abstract)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Sammons et al by specifically using silica to form the coolant lines 14, as taught by Tarnopolsky, because a skilled artisan would have recognized that silica would conduct heat more efficiently than plastic materials, resulting in more effective cooling, and Sammons et al specifically suggested using ceramics for this purpose. As shown by the cited "Crystal quartz (SiO₂) and Fused Silica" website (www.mt-berlin.com), the thermal conductivity and specific heat capacity of silica meet the claim limitations.

Addressing the dependent claims:

Regarding claims 2-5 and 17-20, Sammons discloses polymer sealing means between compartments. (Column 4, lines 36-43)

Regarding claims 6-8 and 21-23, Sammons discloses such housing means comprising ceramic materials. (Figures 2-4, 12 and 14; Column 5, lines 49-55)

Regarding claims 9 and 24, Sammons discloses a general ceramic material, while Tarnopolsky specifically describes cooling lines formed of silica.

Regarding claims 10-13, 32-35, and 38-41, Sammons discloses chambers with an aspect ratio of 1/250. (Column 4, lines 30-34)

Regarding claims 14 and 25, Sammons discloses woven polymer membranes that would be free of such functional groups. (Column 4, lines 44-48)

Regarding claims 27-30, Sammons discloses the first dimension being as low as 2 mm (Column 4, lines 30-34), and it would be a simple matter of design choice to a skilled artisan to reduce this dimension further.

Regarding claims 31, 48, and 49, such variation of compartment dimension would be a matter of selection to one having ordinary skill in the art, absent a showing of criticality.

Regarding claims 36 and 37, Sammons discloses compartments with these dimensions. (Column 4, lines 30-34)

Regarding claims 42-47, Sammons does not specify any particular number of compartments, but explicitly shows 12 compartments in Figure 5, and one having ordinary skill in the art could select any number of compartments (e.g. 50 or more) to meet fractionation and parallel processing requirements.

Regarding claims 55 and 56, Sammons discloses methods meeting all listed limitations. (Column 8, lines 28-39)

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In case the space in any of the preceding boxes is not sufficient.

Claims 1-4, 6-14, 16-19, 21-25, 27-51, and 54-56 lack an inventive step under PCT Article 33(3) as being obvious over Sammons et al in view of the Ettan Daltsix Electrophoresis System manual.

Regarding claims 1, 16, 50, and 51, Sammons et al disclose an electrophoresis apparatus, comprising: an anode and cathode disposed in respective compartments as claimed (Figure 5, 61 and 64) with means for solution addition and removal (e.g. Figure 2, lines 11 and 13) and dimensions as claimed; ion-permeable barriers that prevent convective mixing (17) disposed between compartments; separation compartments disposed between the electrode compartments (Figure 5); and with a portion of each compartment (Cooling lines 14) made from a heat-conductive material, optionally ceramic. (Column 5, lines 49-55)

The Ettan Daltsix Electrophoresis System manual discloses an alumina heat exchanger for removing heat generated by electrophoresis within the system. (Column 1, lines 11-36; Column 2, lines 8-14)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Sammons et al by specifically using alumina to form the coolant lines 14, as taught by the Ettan Daltsix Electrophoresis System manual, because a skilled artisan would have recognized that alumina would conduct heat more efficiently than plastic materials, resulting in more effective cooling, and Sammons et al suggest using a ceramic for this purpose. Since walls of the compartment (16) are defined by the heat exchangers (14) in the system of Sammons et al (Figure 4), this combination would read on the claim. The thermal conductivity and specific heat are properties intrinsic to alumina, and would therefore be present in this combination.

The additional disclosure of Sammons et al is as described previously.

Claims 5 and 20 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied above in addressing claims 4 and 19, and further in view of Chlanda et al.

Sammons et al and Tarnopolsky disclose an apparatus as discussed above in addressing claims 4 and 19. Sammons et al and the Ettan Daltsix Electrophoresis System manual also disclose an apparatus as described above in addressing claims 4 and 19. Sammons et al use silicone rubber for sealing, but suggest using other suitable materials. (Column 4, lines 35-43)

None among Sammons et al, Tarnopolsky, and the Ettan Daltsix Electrophoresis System manual explicitly disclose using any of the listed polymers as sealing means.

Chlanda et al disclose using polyethylene gaskets for sealing chambers within an electrodialysis system. (Column 13, lines 34-37 and 47-51)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the apparatus of Sammons et al by using polyethylene gaskets for sealing chambers, as taught by Chlanda et al, because Sammons suggests using other suitable materials, and Chlanda demonstrates the suitability of this material for this purpose.

Claims 15, 26, 52 and 53 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied above in addressing claims 1, 16, and 51, and further in view of Egen et al

Sammons et al and Tarnopolsky disclose an apparatus as discussed above in addressing claims 1 and 16. Sammons et al and the Ettan Daltsix Electrophoresis System manual disclose an apparatus as described above in addressing claims 1, 16, and 51. Sammons also incorporates US Patent No. 5,173,164 to Egen et al by reference, stating that the apparatus and methods discloses therein are suitable for use within their system. (Column 2, lines 2-6)

None among Sammons et al, Tarnopolsky, and the Ettan Daltsix Electrophoresis System manual explicitly disclose using membranes that are isoelectric barriers.

Egen et al disclose isoelectric focusing within their apparatus, using membranes that could fairly be called isoelectric barriers, given the specific buffer systems specified. (e.g. Column 8, lines 33-49)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the system of Sammons et al by using membranes and buffers suitable for isoelectric focusing, as taught by Egen et al, because Sammons et al explicitly suggest that the methods disclosed by Egen et al are suitable for use in their system.